



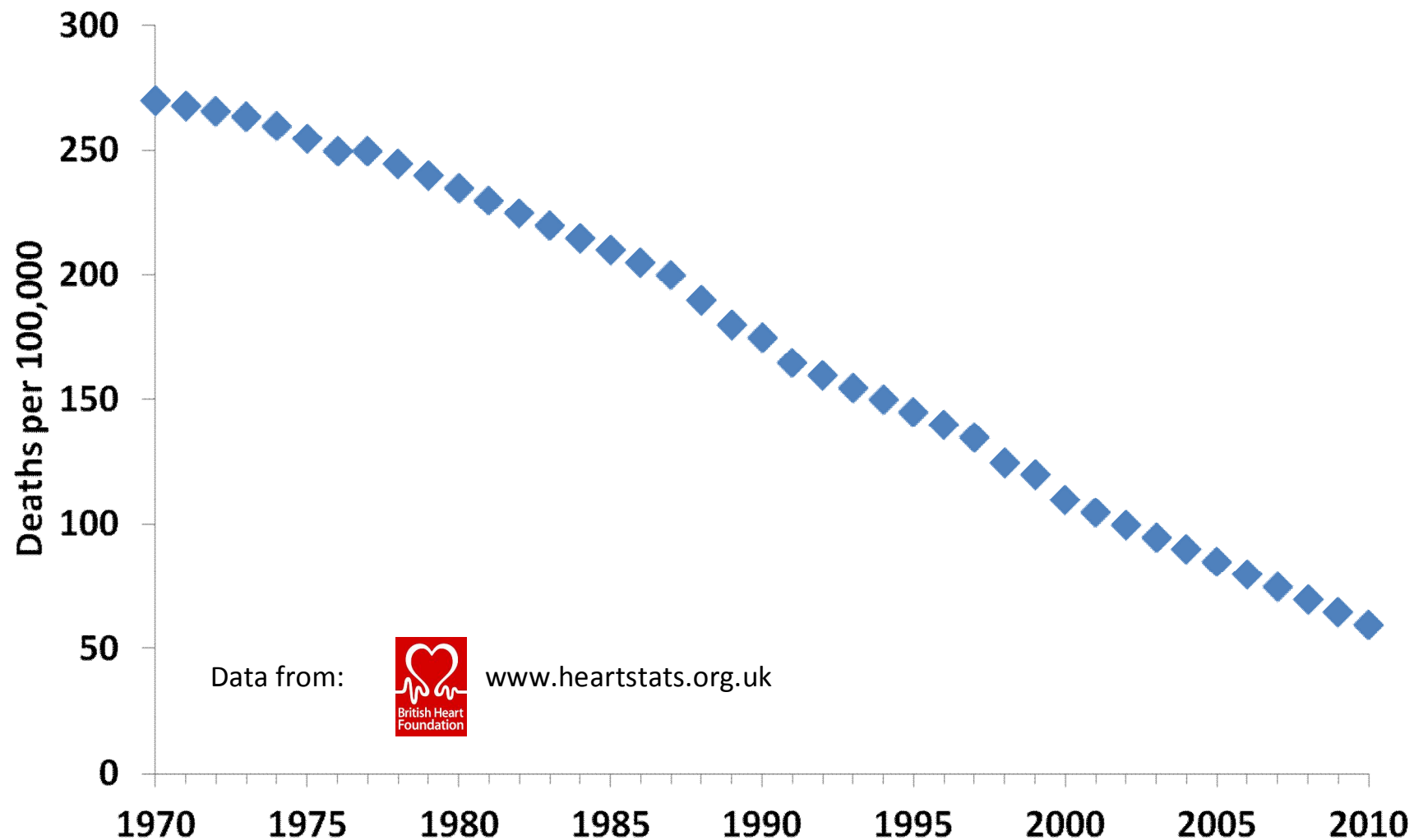
The University of  
Nottingham

# Dietary Fatty Acids and Cardiovascular Disease: Where are we now?

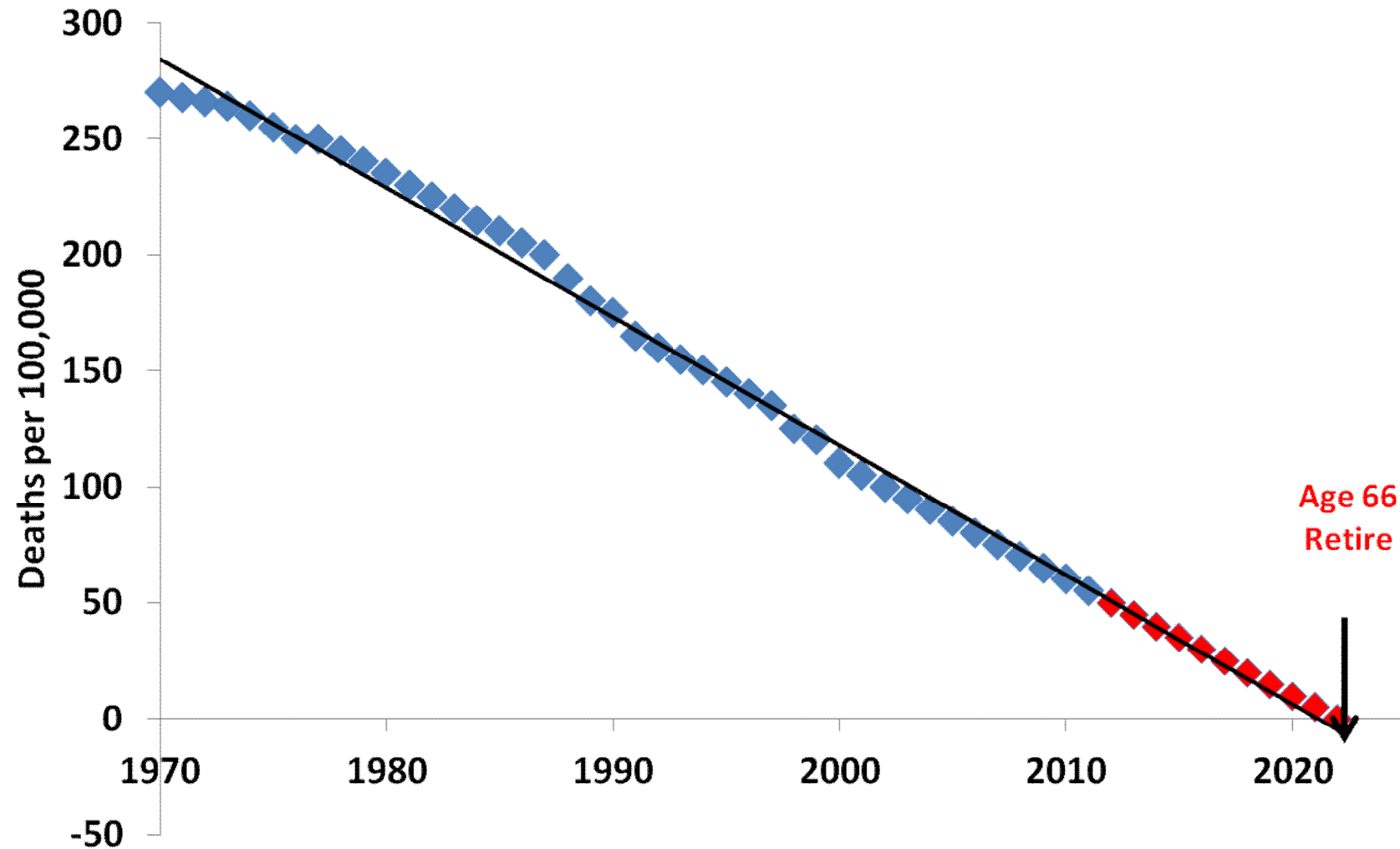
**Professor Andrew Salter  
Division of Nutritional Sciences  
School of Biosciences  
University of Nottingham  
United Kingdom**



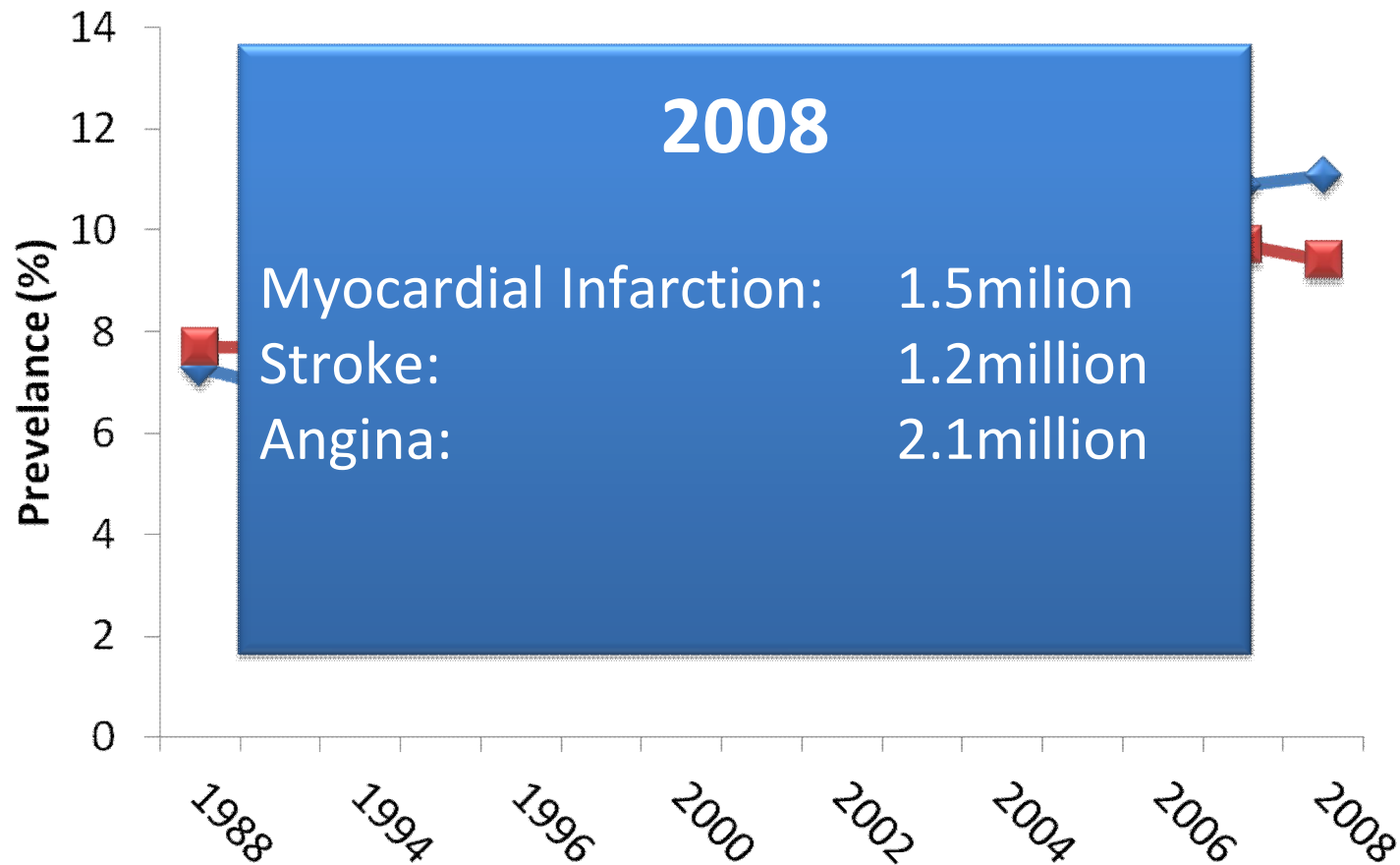
# Age-standardized death rates from CVD, under 75s, 1970-2010, England

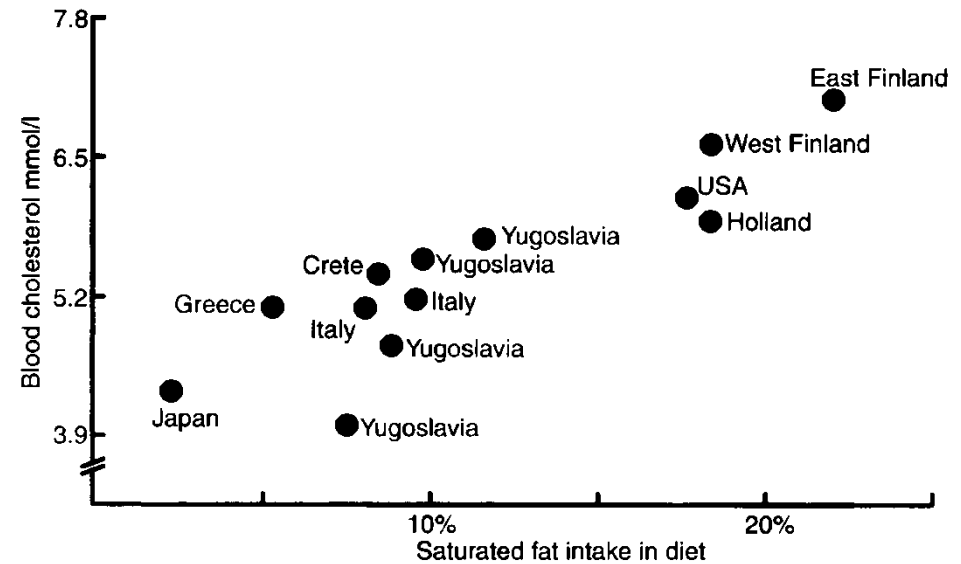
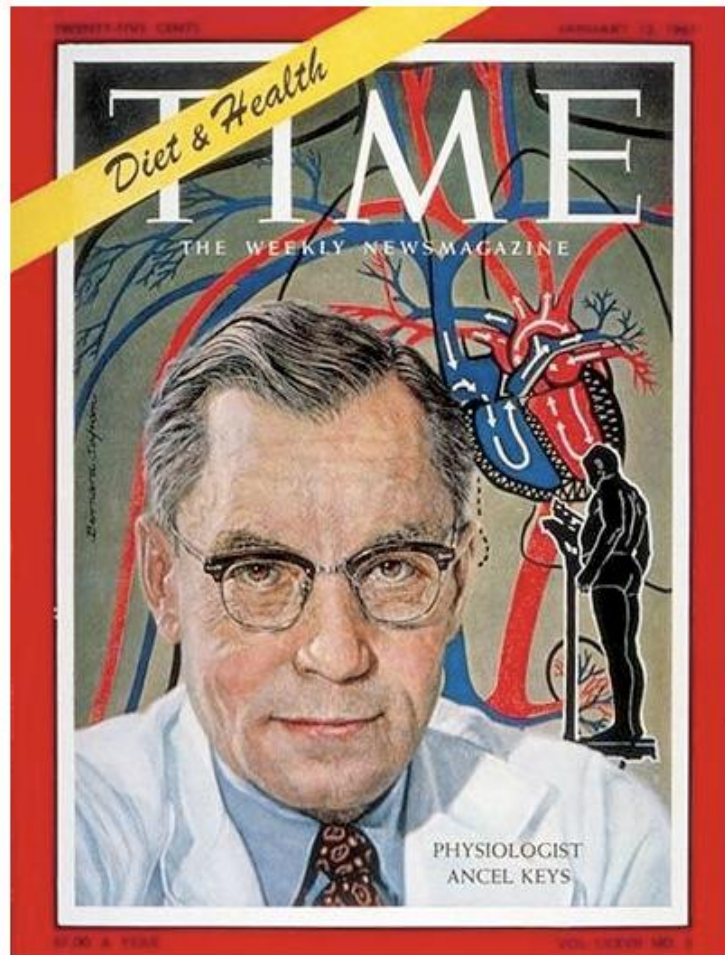


# Age-standardized death rates from CVD, under 75s, 1970-2022, England??



# Prevalence of Cardiovascular disease





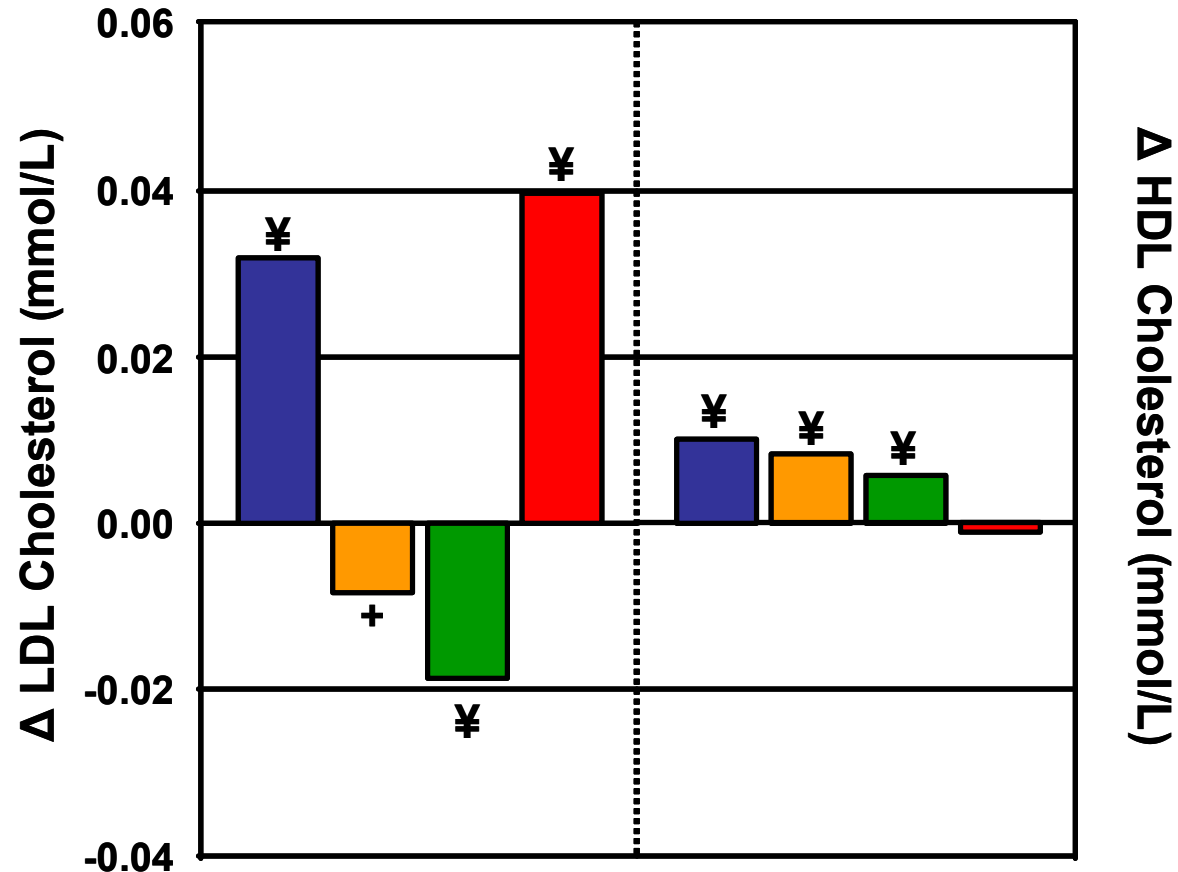
Keys A *et al* (1980) In: Seven countries - a multivariate analysis of death and coronary heart disease. A Commonwealth Fund Book. Cambridge, MA: Harvard University Press, 1-381.

## The Key's Equation

$$\Delta TC = 1.35(2\Delta SFA - \Delta PFA) + 1.5 \Delta CHOL^{1/2}$$

# Meta-Analysis of 60 Trials

$\Delta$  Cholesterol when 1% of carbohydrate energy is replaced with fatty acids



■ Saturated fatty acids

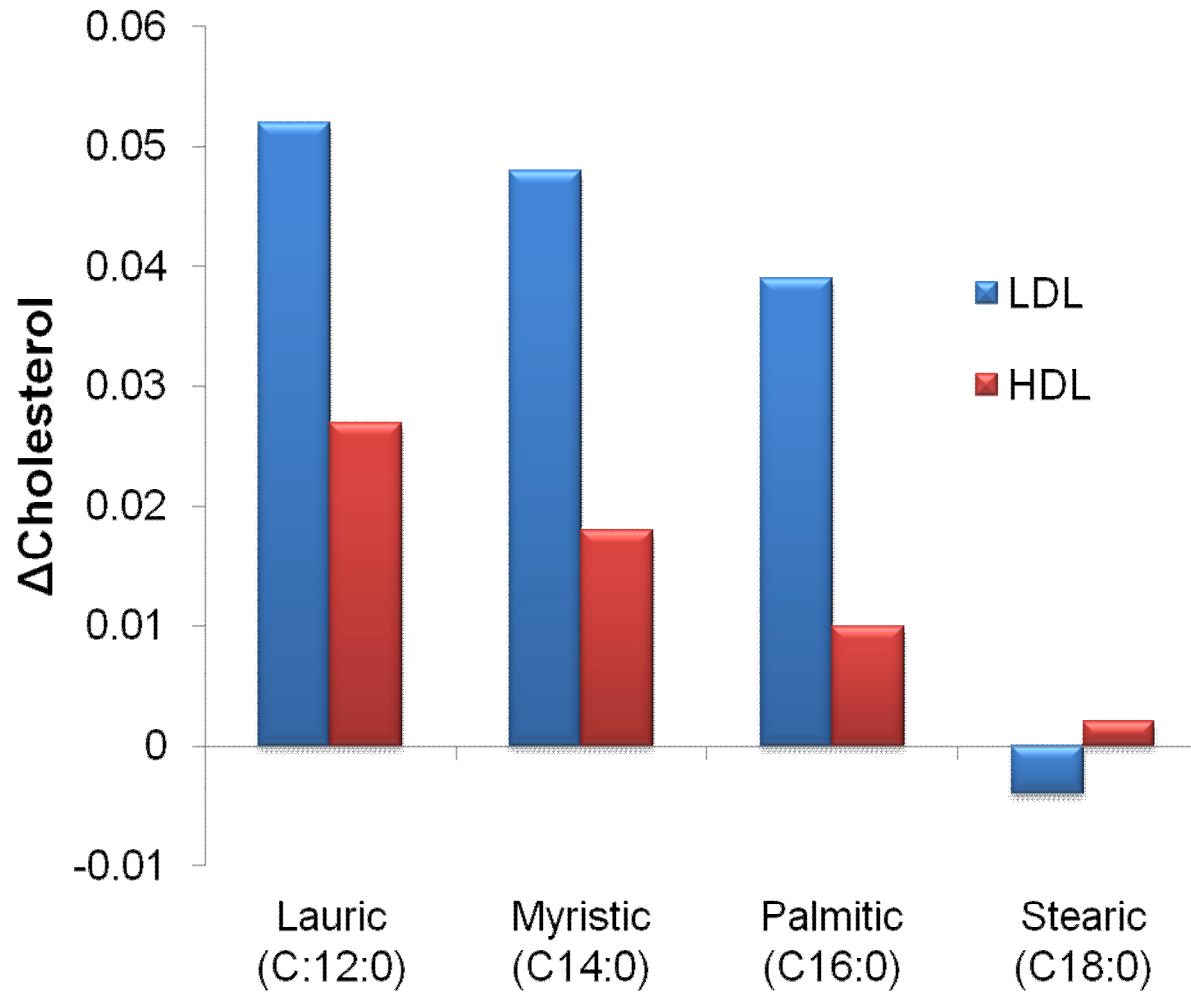
■ *cis* Monounsaturated fatty acids

■ *cis* Polyunsaturated fatty acids

■ *trans* Monounsaturated fatty acids

Mensink et al., 2003

# All Saturates Are Not Equal



Effect of replacing 1% of energy as carbohydrate with different saturated fatty acids  
*-meta-analysis of 60 controlled trials*

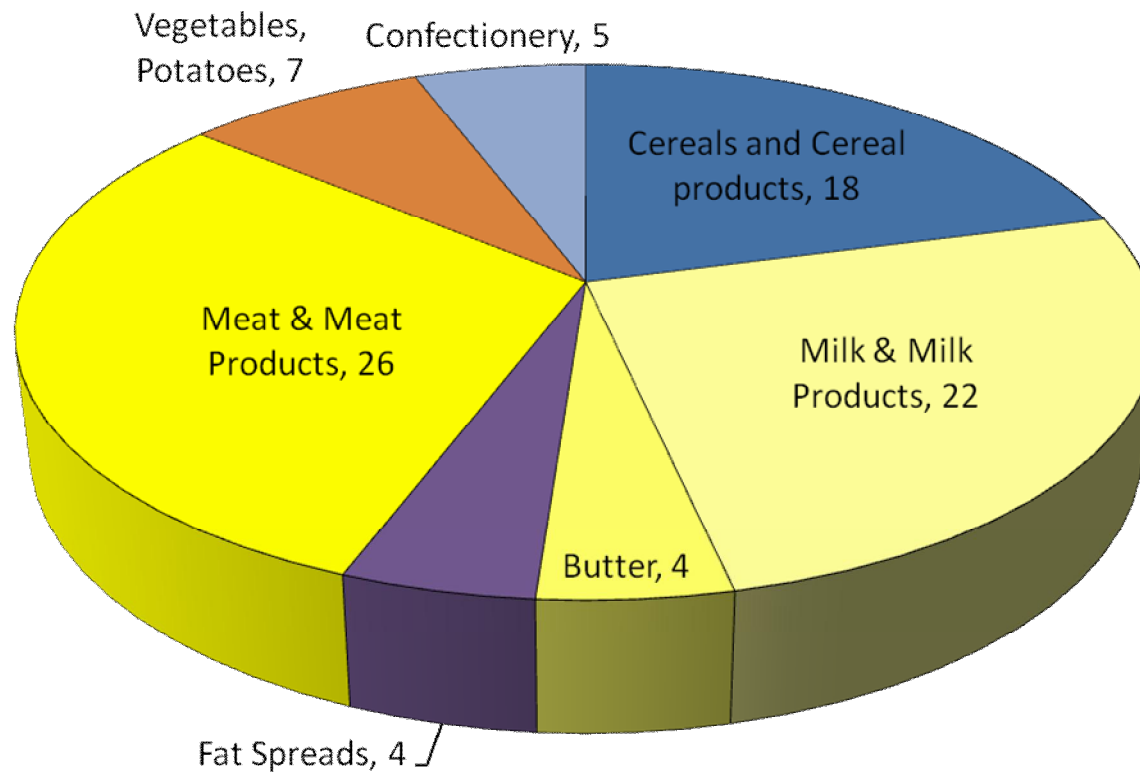
## WHO Adult Recommended Dietary Intakes for Total Fat and Fatty Acids

Fat/Fatty Acid	Recommendation (% of Energy)
Total Fat	20-35
SFA	<10
MUFA	15-20
Total PUFA	6-11
n-6 PUFA	2.5-9
n-3 PUFA	0.5-2
TFA	<1

**Interim Summary of Conclusions and Dietary Recommendations on Total Fat & Fatty Acids  
From the Joint FAO/WHO Expert Consultation on Fats and Fatty Acids in Human Nutrition, 10-  
14  
November, 2008, WHO, Geneva**

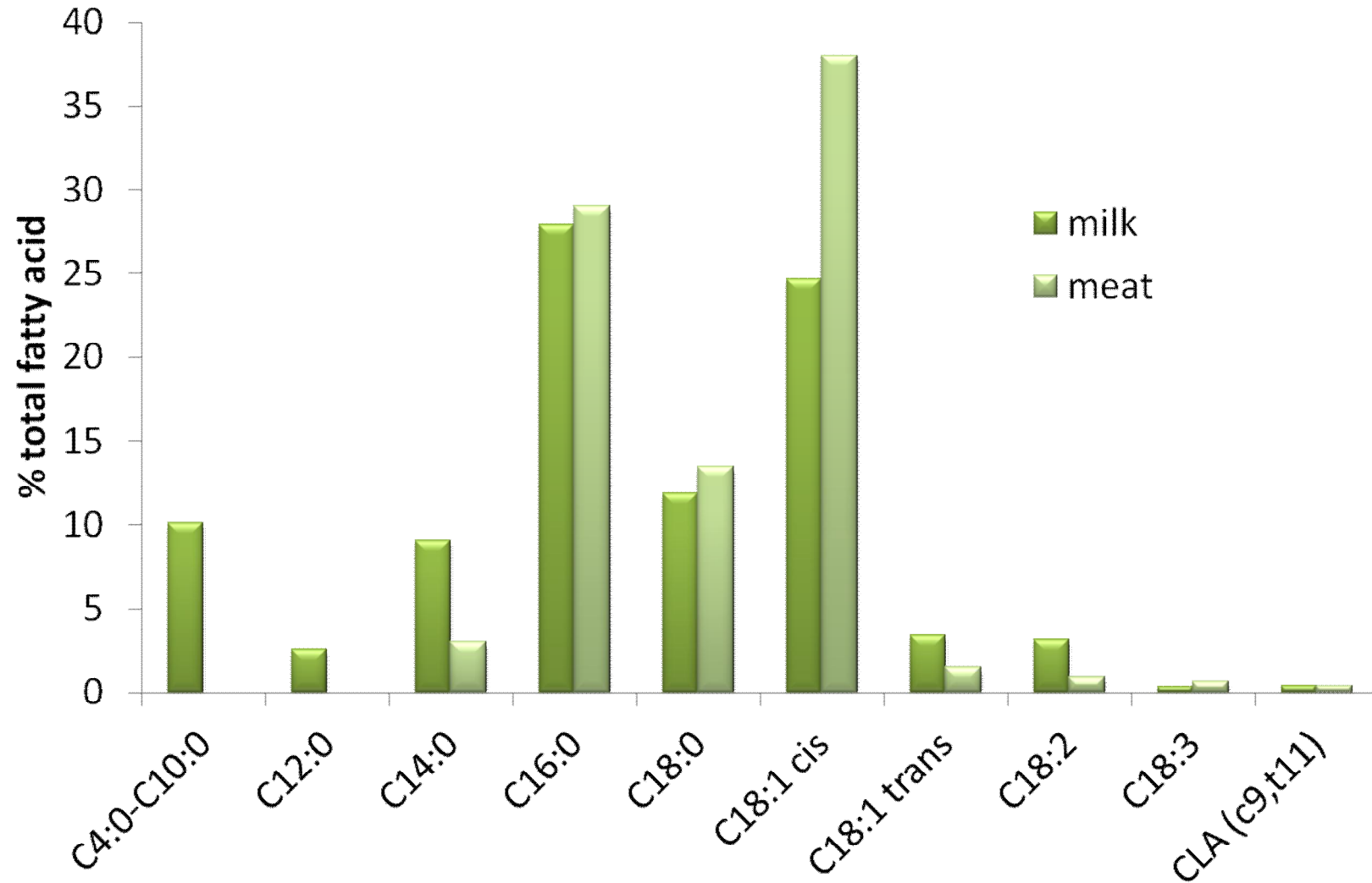


# Sources of Saturated Fatty Acids



National Diet & Nutrition Survey 2008-2009, Dept of Health

# Fatty Acid Composition of Milk and Meat from Ruminant Species



# Meat, Milk & Cardiovascular Disease

- “ Prospective Cohort Studies have generally failed to show any link between red meat consumption and CVD.
- “ Prospective Cohort Studies have, if anything, shown a protective effect of milk consumption on CVD.
- “ **That does not mean that there is no benefit in altering the fatty acid of these foods**

# Epidemiological Studies of Dietary Fat & CVD

## “ Prospective Cohort Studies

- . Large numbers/Long time period
- . Relatively large number of CVD Events
- . Often able to have mortality as outcome
- . Poor measures of dietary intake
- . Highly vulnerable to confounding

## “ Randomized Control

- . More control of dietary intake
- . Measures response to a change
- . Less vulnerable to confounding
- . Smaller numbers/Shorter time periods
- . Smaller number of CVD Events
- . Often rely on risk factors or morbidity as outcome

# Systematic Reviews & Meta-Analyses

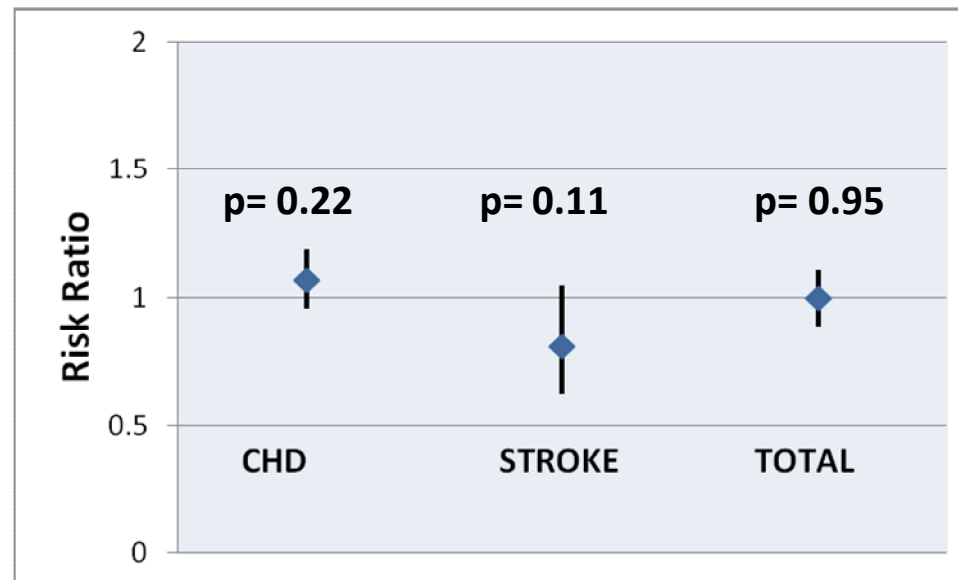
- “ A **systematic review** is a literature review focused on a research question that tries to identify, appraise, select and synthesize all high quality research evidence relevant to that question
- “ **Meta-analysis** combines the results of several studies that address a set of related research hypotheses. In its simplest form, this is normally by identification of a common measure of effect size, for which a weighted average might be the output of a meta-analyses.
- “ **Meta-analyses** are often, but not always, important components of a **systematic review** procedure.

## Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease

Siri-Tarino *et al* (2010) Am J Clin Nutr 91: 535-46

Meta-analysis of 21 studies including 347,747 subjects of whom 11,006 developed CHD or Stroke

**Author's Conclusion:** A meta-analysis of prospective epidemiological studies showed that there is no significant evidence for concluding that dietary saturated fat is associated with an increased risk of CHD or CVD

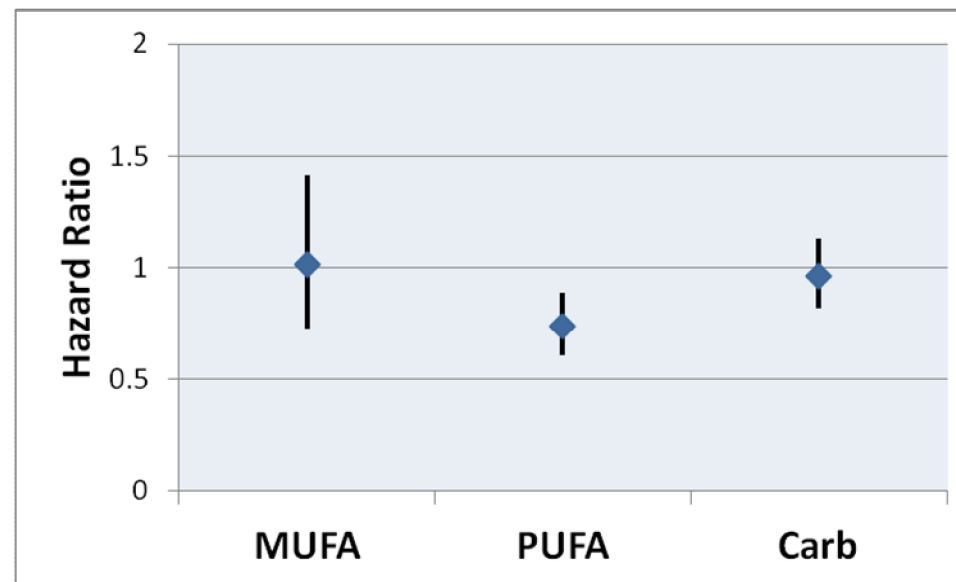


# Major types of dietary fat and risk of coronary heart disease: a pooled analysis of 11 cohort studies

Jakobsen *et al* (2009) *Am J Clin Nutr* 89:1425-32

Hazard Ratio for Coronary Deaths per replacement of 5% energy from SFA with MUFA, PUFA or Carbohydrate

2155 Coronary Deaths among 344696 persons

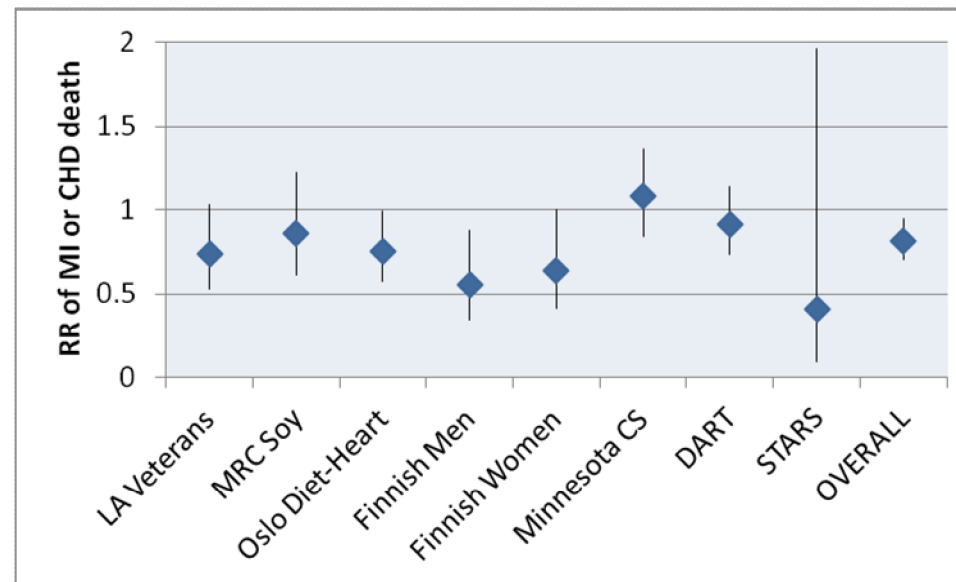


**Author's Conclusion:** Replacing SFAs with PUFA rather than MUFA or Carbohydrates prevents CHD over a wide range of intakes

# Effects on Coronary Heart Disease of Increasing Polyunsaturated Fat in Place of Saturated Fat: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Mozaffarian et al (2010) PLoS Medicine 7: e1000252

8 trials including 13,614 participants with 1,042 CHD Events  
Average PUFA intake - low: 5.0, high: 14.9



**Author's Conclusion:** Consuming PUFA in place of SFA reduces CHD events in RCTs



# Reduced or modified dietary fat for preventing cardiovascular disease

Hooper I *et al* (2011) Cochrane Database of Systematic Reviews  
7: CD002137

- “ 25 studies (61,958 participants) of fat reduction and 15 studies (13,004) of fat modification
- “ No clear effect on total mortality or CVD mortality
- “ 14% decrease in risk of CVD events (RR 0.86, 95%CI 0.77-0.96
  - . Associated with substitution of SFA with UFA not reduction
  - . Related to degree of effect on total and LDL cholesterol
  - . Only in studies of at least 2 years and only in men.

# The New York Times

ON THE WEB

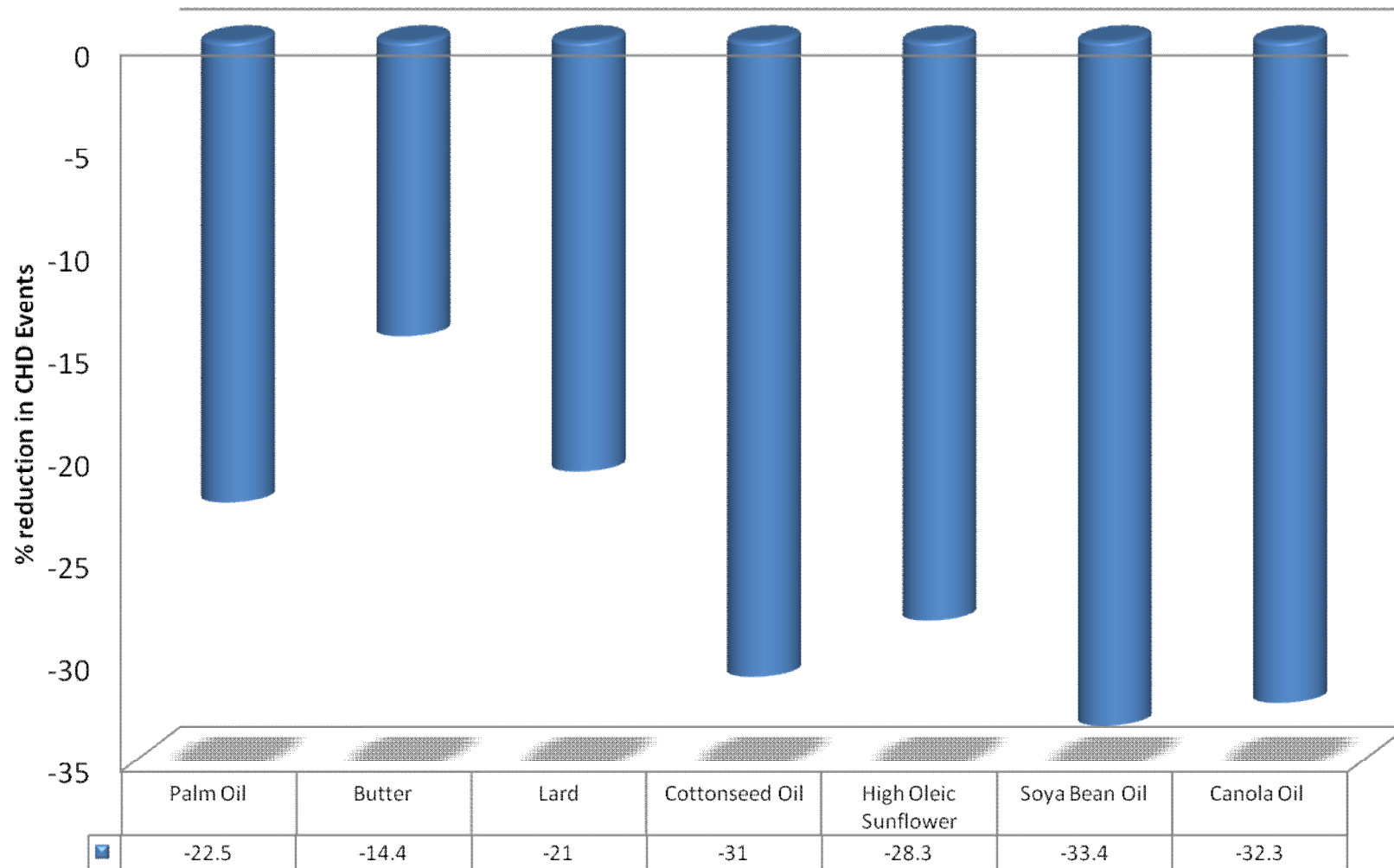
## F.D.A. Announces Label Requirement For Artery Clogger

By MARIAN BURROS (NYT)

Food and Drug Administration will require food processors to include amount of **artery-clogging trans fatty acids** on nutrition labels. Dr. Walter Willett of Harvard School of Public Health suggests that fast food restaurants that serve foods high in trans fats with no warning label may be sued by customers who later have heart attacks; some scientists think trans fats, which are actively added to foods, are at least as bad as saturated fats, and some think trans fats are worse.

# Predicted reduction in CHD Events associated with replacing PHVO with different fats/oils

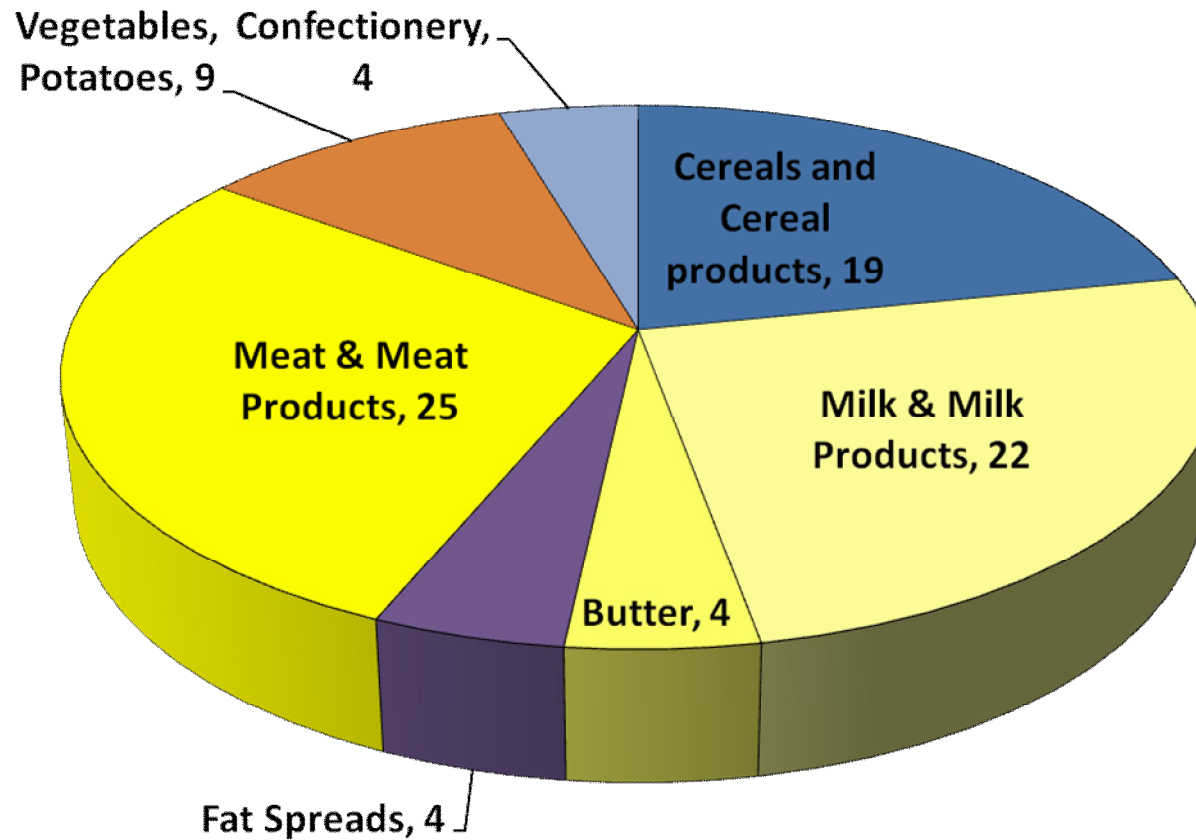
Mozaffarian & Clarke (2009) Eur J Clin Nutr 63: 522-533



Effect of replacing 7.5% of energy from a PHVO containing 35% TFA

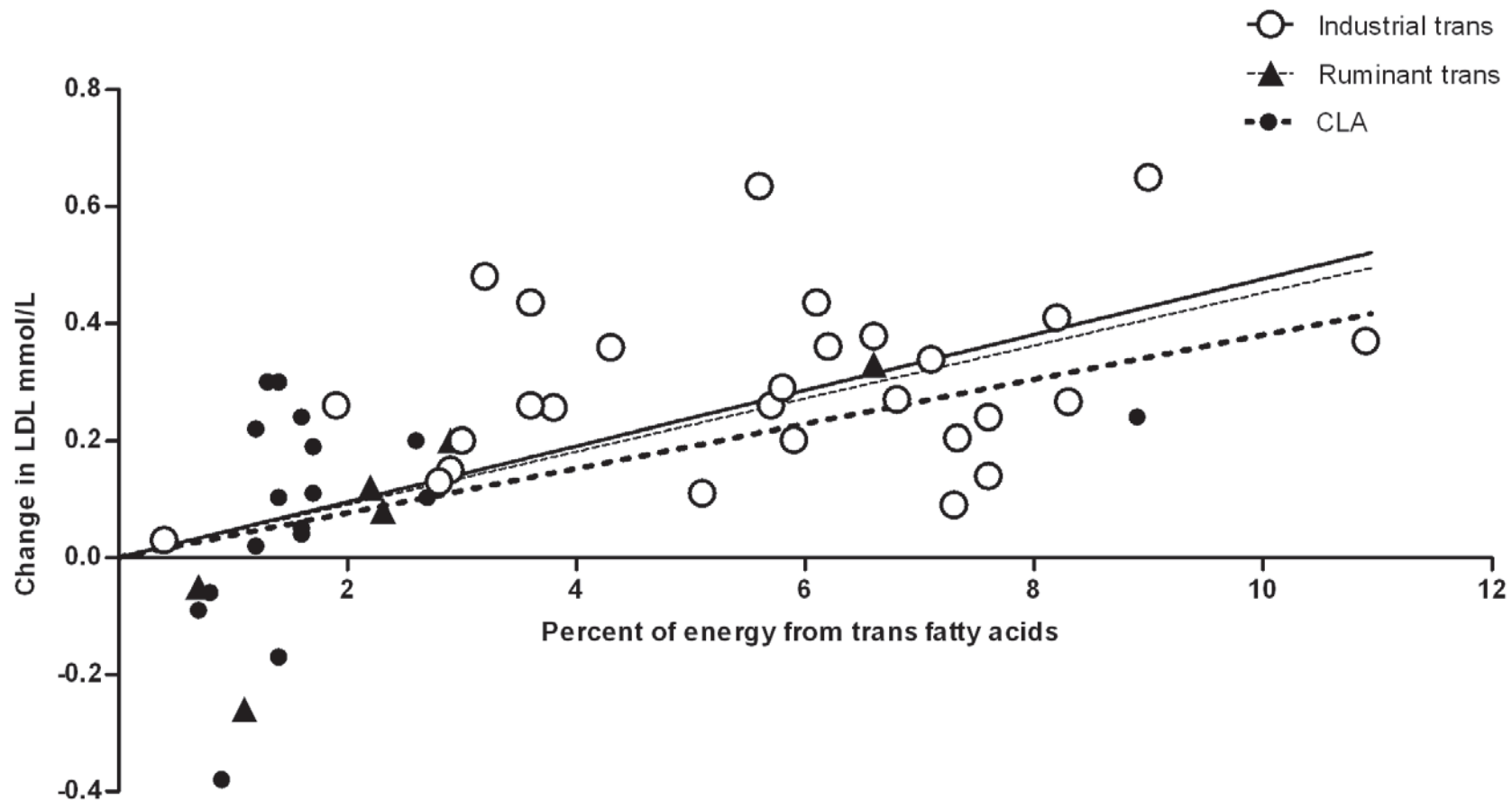
# Sources of *Trans* Fatty Acids

1.6g/day (0.8% food energy)



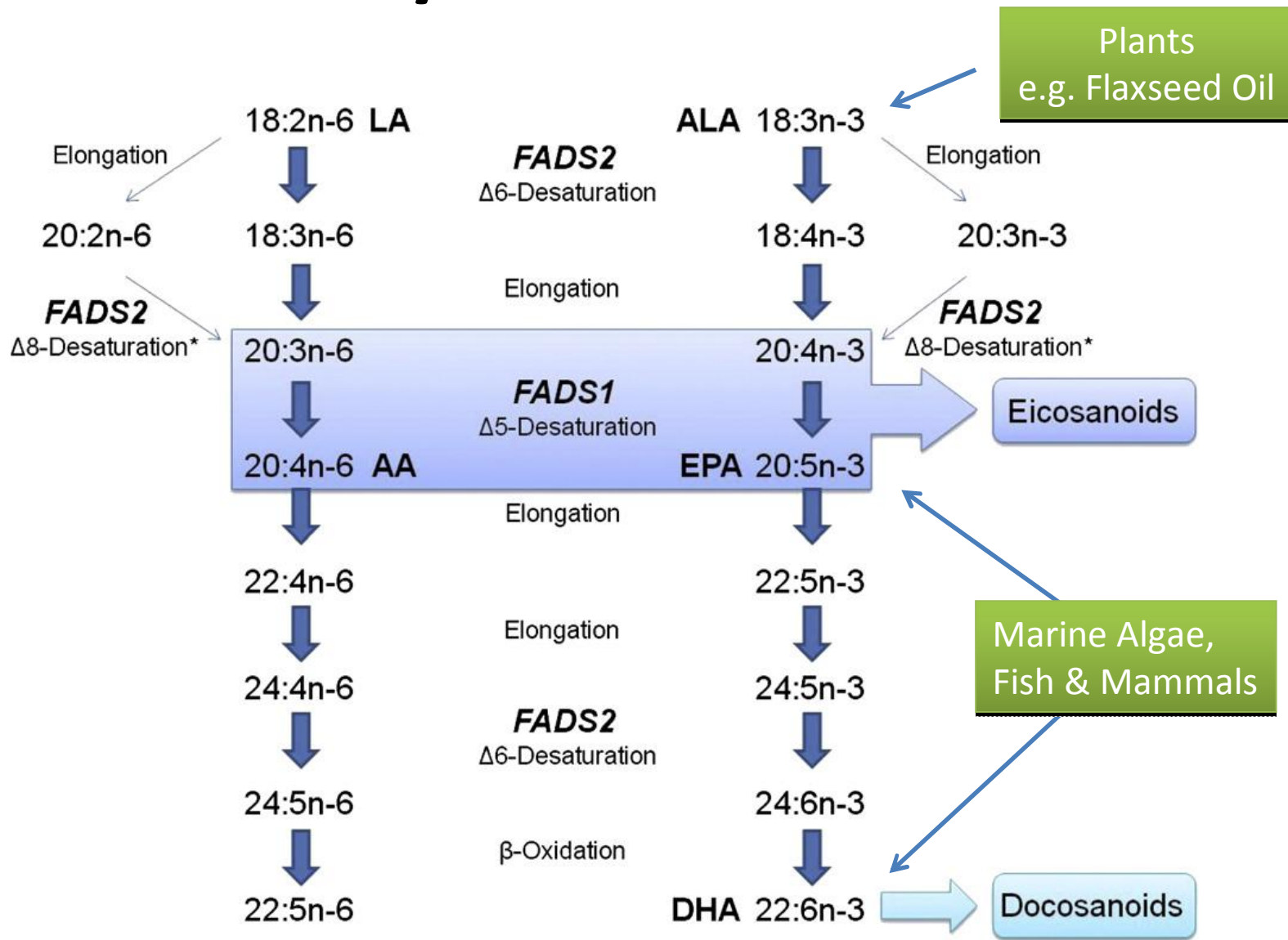
National Diet & Nutrition Survey 2008-2009, Dept of Health

# Meta-Analysis of Impact of trans fatty acids on LDL cholesterol in humans



Citation: Brouwer IA, Wanders AJ, Katan MB (2010) Effect of Animal and Industrial Trans Fatty Acids on HDL and LDL Cholesterol Levels in Humans – A Quantitative Review. PLoS ONE 5(3): e9434. doi:10.1371/journal.pone.0009434

# n-6/n-3 PUFA



# WHO Recommendations on Omega-3 PUFA

“Whilst ALA may have individual properties in its own right, there is evidence that the Omega-3 LCPUFA (EPA & DHA) may contribute to the prevention of CHD and possibly other degenerative diseases of aging. “



Interim Summary of Conclusions and Dietary Recommendations on Total Fat & Fatty Acids. From the Joint FAO/WHO Expert Consultation on Fats and Fatty Acids in Human Nutrition, 10-14 November, 2008, WHO, Geneva

**n-3 Fatty acids from fish or fish-oil supplements, but not  $\alpha$ -linolenic acid, benefit CVD outcomes in primary- and secondary- prevention studies: a systematic review**

*Wang et al (2006) Am J Clin Nutr 84: 5-17*

- “ Review of RCTs, cohort and case control studies of primary and secondary prevention
- “ Increased consumption of n-3 PUFA from fish or fish oil reduces all cause mortality, cardiac and sudden death and, possibly stroke
- “ Evidence better for secondary than primary prevention
- “ No evidence for any beneficial effects of ALA



# Long chain omega-3 dietary supplements and the risk of cardiovascular events: a systematic review.

Marik & Varon (2009) Clin Cardiol 32:365-72.

- “ 11 randomized controlled trials that included a total of 39 044 patients
- “ Included patients after recent myocardial infarction, those with an implanted cardioverter defibrillator, and patients with heart failure, peripheral vascular disease, and hypercholesterolemia
- “ In high risk patients Omega-3 fatty acids (EPA/DHA) significantly reduced the risk of cardiovascular and nonfatal cardiovascular events
- “ **Authors conclusion:** Dietary supplementation with omega-3 fatty acids should be considered in the secondary prevention of cardiovascular events

# Conclusions

“There is little evidence to support replacing dietary SFA with carbohydrate

“Substituting SFA with UFA (Particularly PUFA) reduces risk of CVD

“*Trans* fatty acids associated with Partially Hydrogenated Vegetable Oil increase risk of CVD

“Insufficient evidence to decide whether *trans* fatty acids from animal sources impact on CVD

“There is reasonable evidence that Omega 3 LCPUFA may be important, particularly in secondary prevention of CVD

“Evidence for a role of ALA or n-6/n-3 PUFA ratio less convincing